ring nodes :
1 2 3 4 5 6 7 8 9 19 20 21 22 23 26 27 28 29
chain bonds :
7-18 8-10 9-15 10-11 10-12 12-16 21-24
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 19-21 19-20 20-23 21-22 22-23
22-26 23-29 26-27 27-28 28-29
exact/norm bonds :
5-7 6-9 7-8 7-18 8-9 9-15 10-11 10-12 12-16 19-21 19-20 20-23 21-22
21-24 22-23 22-26 23-29 26-27 27-28 28-29
exact bonds :
8-10
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

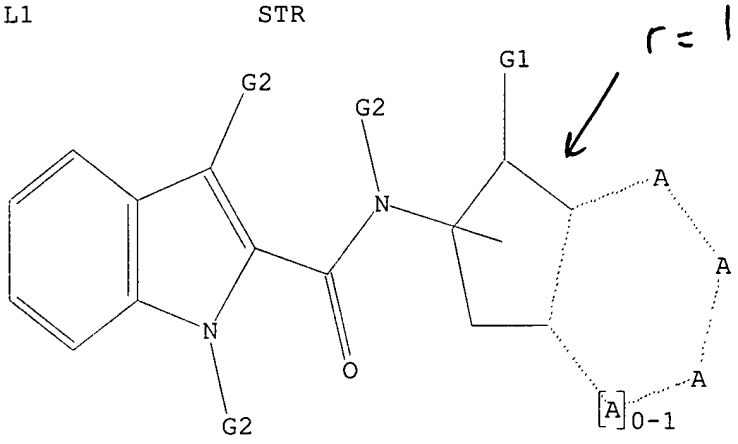
G1:O,N

G2:H,CH3

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 15:CLASS 16:CLASS 18:CLASS 19:Atom 20:Atom 21:Atom
22:Atom 23:Atom 24:CLASS 25:CLASS 26:Atom 27:Atom 28:Atom 29:Atom

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



G1 O,N
G2 H,Me

Structure attributes must be viewed using STN Express query preparation.

=> s l1 full
FULL SEARCH INITIATED 13:34:52 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 294753 TO ITERATE

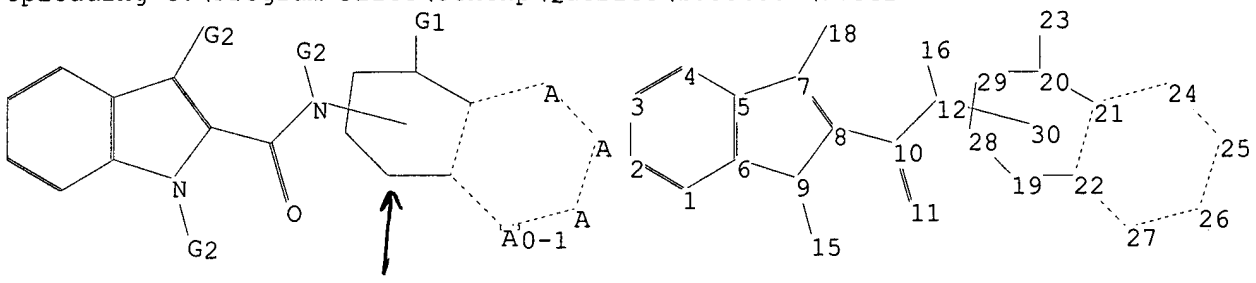
100.0% PROCESSED 294753 ITERATIONS
SEARCH TIME: 00.00.06

99 ANSWERS

L2

L2 99 SEA SSS FUL L1

=>
Uploading C:\Program Files\Stnexp\Queries\10556504\9.str



r=2

chain nodes :
10 11 12 15 16 18 23
ring nodes :
1 2 3 4 5 6 7 8 9 19 20 21 22 24 25 26 27 28 29
chain bonds :
7-18 8-10 9-15 10-11 10-12 12-16 20-23
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 19-22 19-28 20-21 20-29 21-22
21-24 22-27 24-25 25-26 26-27 28-29
exact/norm bonds :
5-7 6-9 7-8 7-18 8-9 9-15 10-11 10-12 12-16 19-22 19-28 20-23 20-21
20-29 21-22 21-24 22-27 24-25 25-26 26-27 28-29
exact bonds :
8-10
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6

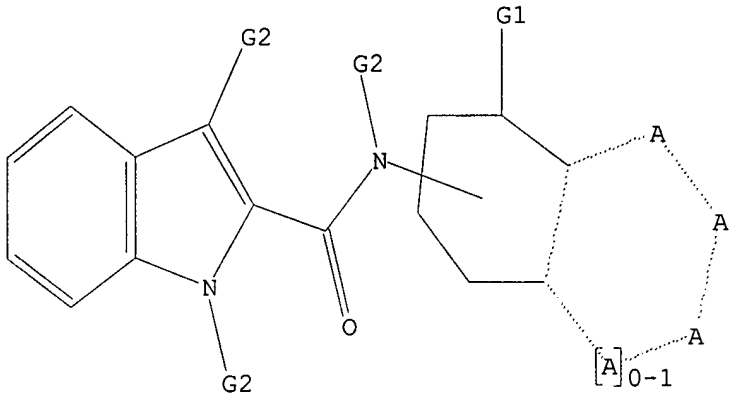
G1:O,N

G2:H,CH3

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:CLASS
11:CLASS 12:CLASS 15:CLASS 16:CLASS 18:CLASS 19:Atom 20:Atom 21:Atom
22:Atom 23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom 28:Atom 29:Atom 30:CLASS

L3 STRUCTURE UPLOADED

=> d
L3 HAS NO ANSWERS
L3 STR



G1 O,N

G2 H,Me

Structure attributes must be viewed using STN Express query preparation.

=> s l3 full
FULL SEARCH INITIATED 13:36:25 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 294753 TO ITERATE

100.0% PROCESSED 294753 ITERATIONS 37 ANSWERS
SEARCH TIME: 00.00.05

L4 37 SEA SSS FUL L3

L4

=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	335.20	335.41

FILE 'CAPLUS' ENTERED AT 13:37:30 ON 15 FEB 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 15 Feb 2006 VOL 144 ISS 8
FILE LAST UPDATED: 14 Feb 2006 (20060214/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l2
L5 3 L2

=> s l4
L6 5 L4

=> s l5 or l6
L7 8 L5 OR L6

=> d ibib abs hitstr 1-8

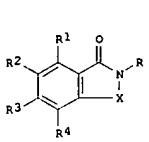
L7 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1103563 CAPLUS
DOCUMENT NUMBER: 143:387025
TITLE: Preparation of aromatic or heterocycle imine and amide
derivatives as prostaglandin D2 (PGD2) production inhibitors
INVENTOR(S): Tanaka, Rika; Kitagawa, Hirohisa; Sasaki, Masao; Muto,
Susumu; Itai, Akiko; Tokuyama, Ryukou
PATENT ASSIGNEE(S): Institute of Medicinal Molecular Design. Inc., Japan
SOURCE: PCT Int. Appl., 232 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

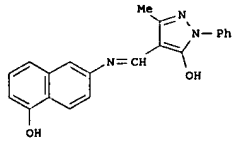
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005094805	A1	20051013	WO 2005-JP6464	20050401

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2004-108702 A 20040401

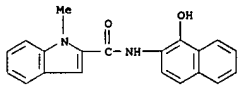
OTHER SOURCE(S): MARPAT 143:387025
GI


II


IV

AB There is provided a medicine having prostaglandin D2 (PGD2) production inhibitory activity and having as an active ingredient a substance

L7 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
selected from compds. represented by the general formula A-Y-B (I) (herein
A and B each independently represents an optionally substituted, cyclic hydrocarbon or heterocyclic group; Y represents -CH= N-, -N=CH-, -CONH-, or -NHCO-, provided that the compds. represented by the following formula (II) [wherein X represents the formula -N= C(R5)- (wherein the left-side bond is bonded to the benzene ring and the right-side bond is bonded to the nitrogen atom) or the formula -NHCH(R5)- (wherein the left-side bond is bonded to the benzene ring and the right-side bond is bonded to the nitrogen atom); R1, R2, R3, and R4 each independently represents hydrogen,
halogeno, or optionally substituted C1-6 alkyl or hydroxy; R5 represents an optionally substituted C1-6 alkyl or C6-10 aryl group; R represents optionally substituted amino] are excluded] salts, hydrates, and solvates thereof. These drugs contg. the compds. I possess antiallergic, antiallergic-inflammatory, antiasthmatic, cerebral protective, sexual cycle-regulating, sleep-regulating, body temp.-regulating, analgesic, olfaction-regulating activities and activities for preventing the worsening of brain injuries or for improving brain after brain injuries. They also possess the inhibitory activity against the prodn. of hematopoietic prostaglandin D2. Thus, a soln. of 2.90 g 3-methyl-1-phenyl-4,5-dihydropyrazol-5-one in 4 mL DMF was treated with 1.85 mL POCl3 under ice-cooling, stirred at 80° for 1 h, and cooled to room temp., and the reaction mixt. was poured into ice water, stirred at room temp. overnight, filtered t give, after washing the product with water, drying, and washing with iso-Pr ether, 50% 3-methyl-5-oxo-1-phenyl-
4,5-dihydropyrazole-4-carboxaldehyde (III). A mixt. of the compd. III (222 mg), 159 mg 5-amino-1-naphthol, and 5 mL ethanol was refluxed for 30 min, cooled to room temp., and filtered to give, after washing with ethanol, 88% 5-hydroxy-1-phenyl-3-methyl-4-[[(1-hydroxy-6-naphthyl)imino]methyl]pyrazole (IV). The compd. IV at 10 μM inhibited >99% the prodn. of PGD2 in rat basophil leukemia cells RBL-2H3 expressing hematopoietic PGD2 synthetase.
IT **866469-48-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aromatic or heterocycle imine and amide derivs. as prostaglandin D2 (PGD2) production inhibitors for drugs)
RN 866469-48-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-(1-hydroxy-2-naphthalenyl)-1-methyl- (9CI) (CA
INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

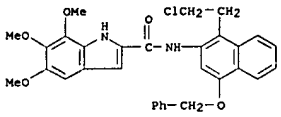
L7 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:383225 CAPLUS
DOCUMENT NUMBER: 143:70994
TITLE: A Novel Class of in Vivo Active Anticancer Agents: Achiral seco-Amino- and seco-Hydroxycyclopropylbenz[e]indolone (seco-CBI) Analogues
of the Duocarmycins and CC-1065
AUTHOR(S): Sato, Atsushi; McNulty, LuAnne; Cox, Kari; Kim, Susan;
Scott, Adrienne; Daniell, Kristen; Summerville, Kaitlin; Price, Carly; Hudson, Stephen; Kiakos, Konstantinos; Hartley, John A.; Asao, Tetsuji; Lee, Moses
CORPORATE SOURCE: Department of Chemistry, Furman University, Greenville, SC, 29613, USA
SOURCE: Journal of Medicinal Chemistry (2005), 48(11), 3903-3918
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

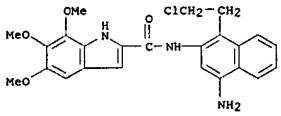
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB One achiral seco-hydroxycyclopropylbenz[e]indolone (seco-CBI) (I) and seven achiral seco-amino-CBI analogs of CC-1065 and the duocarmycins (e.g.
II) were designed, synthesized and evaluated for their DNA-binding and anticancer properties. These compds. contain a core 2-chloroethylnaphthalene structure and they do not have a stereo-center. From thermal cleavage gel analyses, the seven achiral compds. and I demonstrated similar covalent sequence specificity to adozelesin and the racemic seco-CBI-TMI (III) for binding to the 5'-AAAAA(865)-3' site. Continuous exposure of human (K562) and murine (B16, L1210 and P815) cancer cell lines to the compds. demonstrated their significant cytotoxicity, with IC50 values in the sub-micromolar range. Generally, a good leaving group on the Et moiety and a free amino or hydroxyl group on the naphthyl moiety are essential for activity. According to NCI's cytotoxicity screen, compds. II and I were active against human cancer cell lines derived from lung, colon, melanoma, renal system, and breast. At the resp. doses of 15 and 20 mg/kg (administered via an i.p. route), compds. II and I inhibited the growth of murine B16-F0 melanoma in C57BL/6
mice, with minimal toxicity, and II gave a significant anticancer effect. The in vivo anticancer activity of compound II was confirmed in a human tumor xenograft study (advanced stage SC-OVCAR-3 ovarian cancer growing in
scid mice). Finally, compound II was not toxic to murine bone marrow cell
growth in culture at a dose that was toxic for the previously reported compound III.
IT **413578-28-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

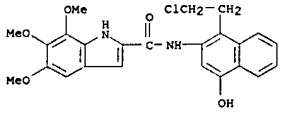
L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
(novel class of in vivo active anticancer agents and achiral seco-amino- and seco-hydroxycyclopropylbenz[e]indolone (seco-CBI) analogs of duocarmycins and CC-1065)
RN 413578-28-6 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-chloroethyl)-4-(phenylmethoxy)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



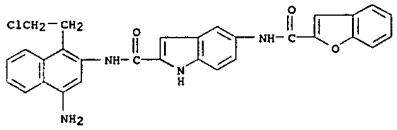
IT **413577-16-9P 413577-17-0P 413577-83-0P 413577-87-4P 413577-94-3P 413578-14-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel class of in vivo active anticancer agents and achiral seco-amino- and seco-hydroxycyclopropylbenz[e]indolone (seco-CBI) analogs of duocarmycins and CC-1065)
RN 413577-16-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-chloroethyl)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



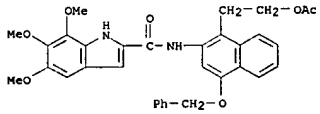
RN 413577-17-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-chloroethyl)-4-hydroxy-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



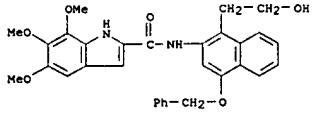
L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



IT **413578-25-3P 413578-26-4P 413578-27-5P 855299-65-9P 855299-66-0P 855299-67-1P 855299-68-2P 855299-69-3P 855299-70-6P 855299-71-7P 855299-72-8P 855299-73-9P 855299-74-0P 855299-75-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(novel class of in vivo active anticancer agents and achiral seco-amino- and seco-hydroxycyclopropylbenz[e]indolone (seco-CBI) analogs of duocarmycins and CC-1065)
RN 413578-25-3 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[2-(acetyloxy)ethyl]-4-(phenylmethoxy)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



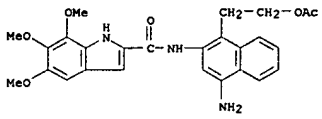
RN 413578-26-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-hydroxyethyl)-4-(phenylmethoxy)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



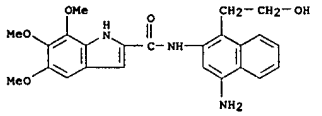
RN 413578-27-5 CAPLUS
CN 1H-Indole-2-carboxamide, 5,6,7-trimethoxy-N-[1-[2-[(methylsulfonyl)oxy]ethyl]-4-(phenylmethoxy)-2-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

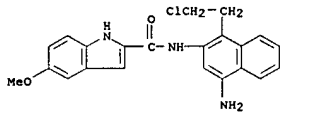
RN 413577-83-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[2-(acetyloxy)ethyl]-4-amino-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



RN 413577-87-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-hydroxyethyl)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)

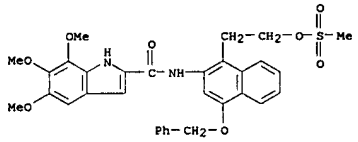


RN 413577-94-3 CAPLUS
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-chloroethyl)-2-naphthalenyl]-5-methoxy- (9CI) (CA INDEX NAME)

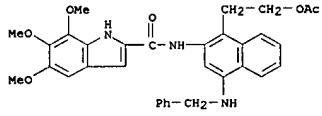


RN 413578-14-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-chloroethyl)-2-naphthalenyl]-5-[(2-benzofuranylcarbonyl)amino]- (9CI) (CA INDEX NAME)

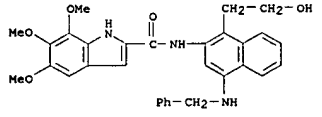
L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



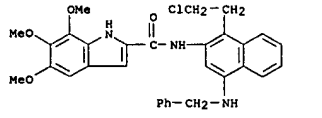
RN 855299-65-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[2-(acetyloxy)ethyl]-4-[(phenylmethyl)amino]-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



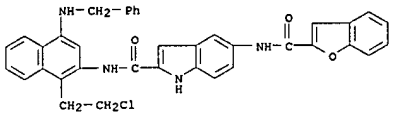
RN 855299-66-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-hydroxyethyl)-4-[(phenylmethyl)amino]-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



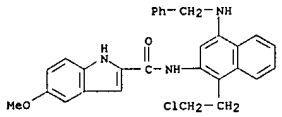
RN 855299-67-1 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-chloroethyl)-4-[(phenylmethyl)amino]-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



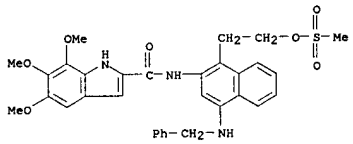
L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 855299-68-2 CAPLUS
CN 1H-Indole-2-carboxamide, 5-[(2-benzofuranylcarbonyl)amino]-N-[1-(2-chloroethyl)-4-[(phenylmethyl)amino]-2-naphthalenyl]- (9CI) (CA INDEX NAME)



RN 855299-69-3 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-chloroethyl)-4-[(phenylmethyl)amino]-2-naphthalenyl]-5-methoxy- (9CI) (CA INDEX NAME)

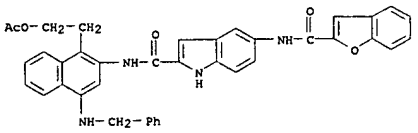


RN 855299-70-6 CAPLUS
CN 1H-Indole-2-carboxamide, 5,6,7-trimethoxy-N-[1-[2-[(methylsulfonyl)oxy]ethyl]-4-[(phenylmethyl)amino]-2-naphthalenyl]- (9CI) (CA INDEX NAME)

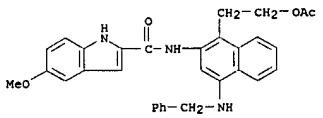


RN 855299-71-7 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[2-(acetyloxy)ethyl]-4-[(phenylmethyl)amino]-2-naphthalenyl]-5-[(2-benzofuranylcarbonyl)amino]- (9CI) (CA INDEX NAME)

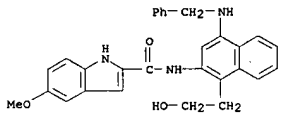
L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 855299-72-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[2-(acetyloxy)ethyl]-4-[(phenylmethyl)amino]-2-naphthalenyl]-5-methoxy- (9CI) (CA INDEX NAME)

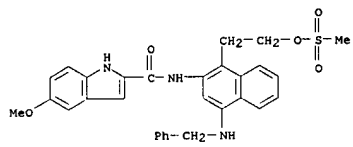


RN 855299-73-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-hydroxyethyl)-4-[(phenylmethyl)amino]-2-naphthalenyl]-5-methoxy- (9CI) (CA INDEX NAME)

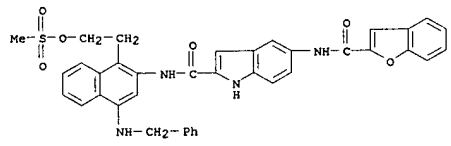


RN 855299-74-0 CAPLUS
CN 1H-Indole-2-carboxamide, 5-methoxy-N-[1-[2-[(methylsulfonyl)oxy]ethyl]-4-[(phenylmethyl)amino]-2-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 855299-75-1 CAPLUS
CN 1H-Indole-2-carboxamide, 5-[(2-benzofuranylcarbonyl)amino]-N-[1-[2-[(methylsulfonyl)oxy]ethyl]-4-[(phenylmethyl)amino]-2-naphthalenyl]- (9CI) (CA INDEX NAME)

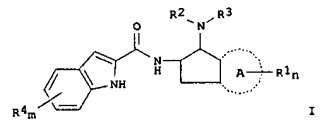


REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

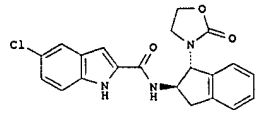
L7 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:216668 CAPLUS
DOCUMENT NUMBER: 142:297984
TITLE: Preparation of indole-2-carboxamide derivatives as glycogen phosphorylase inhibitors
INVENTOR(S): Bennett, Stuart Norman Lile; Simpson, Iain
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005020985	A1	20050310	WO 2004-GB3620	20040825
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			GB 2003-20242	A 20030829
			GB 2004-1800	A 20040128

OTHER SOURCE(S): MARPAT 142:297984
GI



I

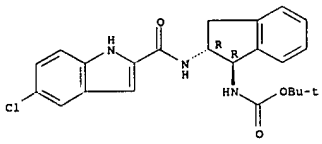


II

AB Title compds. represented by the formula I [wherein A = phenylene or heteroarylene; n = 0-2; m = 0-2; R1 = independently halo, NO2, CN,

L7 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
carbamoyl, etc.; R2R3 = (un)substituted heterocyclic ring; R4 = independently halo, OH, carboxy, etc.; with a proviso; and pharmaceutically acceptable salts or prodrugs thereof] were prepd. as glycogen phosphorylase inhibitors (no data). For example, II was given in
a multi-step synthesis starting from 5-chloroindole-2-carboxylic acid. I and their pharmaceutical compns. are useful as glycogen phosphorylase inhibitors for the treatment of disease states assocd. with increased glycogen phosphorylase activity (no data).
IT **597555-50-5P 846542-86-7P 847658-36-0P**
847658-37-1P 847658-38-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of N-indenyl indole-2-carboxamide derivs. as glycogen phosphorylase inhibitors)
RN 597555-50-5 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

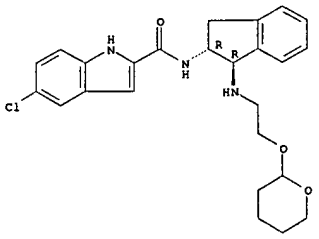
Absolute stereochemistry.



RN 846542-86-7 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[[2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

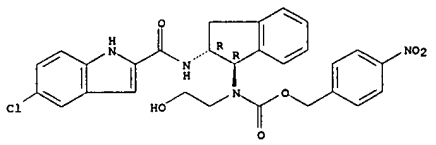
Absolute stereochemistry.

L7 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 847658-36-0 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl](2-hydroxyethyl)-, (4-nitrophenyl)methyl ester (9CI)
(CA INDEX NAME)

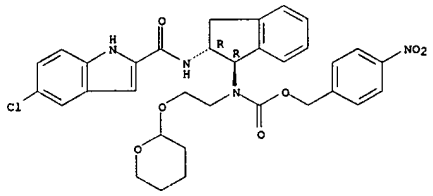
Absolute stereochemistry.



RN 847658-37-1 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl][2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]-, (4-nitrophenyl)methyl ester (9CI) (CA INDEX NAME)

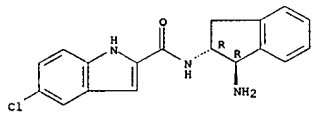
Absolute stereochemistry.

L7 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 847658-38-2 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-amino-2,3-dihydro-1H-inden-2-yl]-5-chloro-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	2005:182625 CAPLUS
DOCUMENT NUMBER:	142:261398
TITLE:	Preparation of indole-2-carboxamide derivatives as glycogen phosphorylase inhibitors
INVENTOR(S):	Bennett, Stuart Norman Lile; Simpson, Iain; Whittamore, Paul Robert Owen
PATENT ASSIGNEE(S):	Astrazeneca Ab, Swed.; Astrazeneca Uk Limited
SOURCE:	PCT Int. Appl., 74 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

Same Inventors

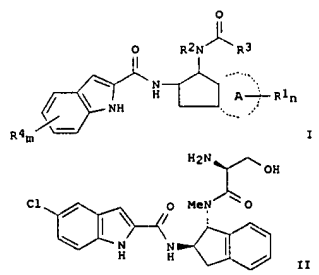
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005019172	A1	20050303	WO 2004-GB3552	20040818

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		GB 2003-19690	A 20030822
OTHER SOURCE(S):	MARPAT 142:261398		

GI



I

II

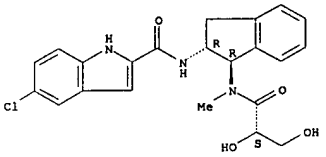
AB Title compds. represented by the formula I [wherein A = phenylene or

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
heteroarylene; n = 0-2; m = 0-2; R1 = independently halo, NO2, CN, carbamoyl, etc.; R2, R3 = independently (halo)alkyl, CF3, hydroxyalkyl, etc.; R4 = independently halo, OH, carboxy, etc.; and pharmaceutically acceptable salts or prodrugs thereof] were prepd. as glycogen phosphorylase inhibitors. For example, II•HCl was given in a multi-step synthesis starting from 5-chloroindole-2-carboxylic acid. II showed 173 μM thermodn. soly. and plasma protein binding activity with Ki value of 0.5 μM. Thus, I and their pharmaceutical compns. are useful as glycogen phosphorylase inhibitors for the treatment of disease states assocd. with increased glycogen phosphorylase activity.

IT 846542-52-7P 846542-53-8P 846542-54-9P
846542-55-0P 846542-56-1P 846542-57-2P
846542-58-3P 846542-59-4P 846542-60-7P
846542-61-8P 846542-62-9P 846542-63-0P
846542-64-1P 846542-65-2P 846542-67-4P
846542-68-5P 846542-69-6P 846542-70-9P
846542-71-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of indole-2-carboxamide derivs. as glycogen phosphorylase inhibitors)

RN 846542-52-7 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-1-[[(2S)-2,3-dihydroxy-1-oxopropyl]methylamino]-2,3-dihydro-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

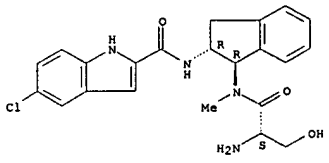
Absolute stereochemistry.



RN 846542-53-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-[[(2S)-2-amino-3-hydroxy-1-oxopropyl]methylamino]-2,3-dihydro-1H-inden-2-yl]-5-chloro-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

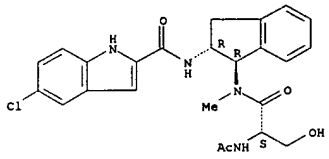
L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● HCl

RN 846542-54-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-[[(2S)-2-(acetylamino)-3-hydroxy-1-oxopropyl]methylamino]-2,3-dihydro-1H-inden-2-yl]-5-chloro- (9CI) (CA INDEX NAME)

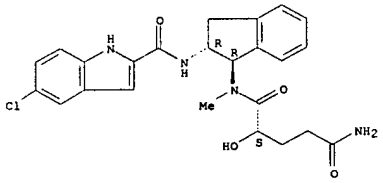
Absolute stereochemistry.



RN 846542-55-0 CAPLUS
CN Pentanediamide, N-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-2-hydroxy-N-methyl-, (2S)- (9CI) (CA INDEX NAME)

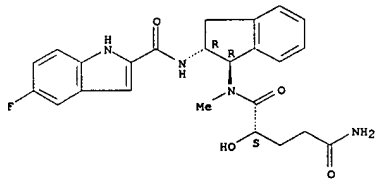
Absolute stereochemistry.

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



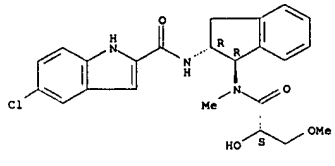
RN 846542-56-1 CAPLUS
CN Pentanediamide, N-[(1R,2R)-2-[[(5-fluoro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-2-hydroxy-N-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 846542-57-2 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[[(2S)-2-hydroxy-3-methoxy-1-oxopropyl]methylamino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

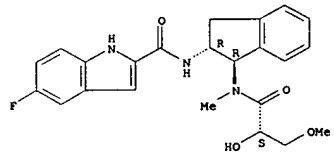
Absolute stereochemistry.



RN 846542-58-3 CAPLUS

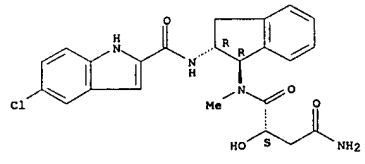
L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-2,3-dihydro-1-[[(2S)-2-hydroxy-3-methoxy-1-oxopropyl]methylamino]-1H-inden-2-yl]-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



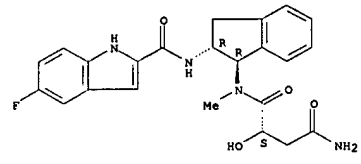
RN 846542-59-4 CAPLUS
CN Butanediamide, N1-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-2-hydroxy-N1-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 846542-60-7 CAPLUS
CN Butanediamide, N1-[(1R,2R)-2-[[(5-fluoro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-2-hydroxy-N1-methyl-, (2S)- (9CI) (CA INDEX NAME)

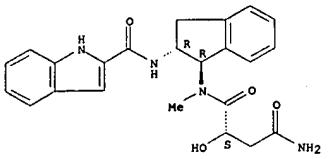
Absolute stereochemistry.



L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

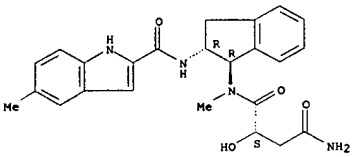
RN 846542-61-8 CAPLUS
CN Butanediamide, N1-[(1R,2R)-2,3-dihydro-2-[(1H-indol-2-ylcarbonyl)amino]-1H-inden-1-yl]-2-hydroxy-N1-methyl-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 846542-62-9 CAPLUS
CN Butanediamide, N1-[(1R,2R)-2,3-dihydro-2-[[(5-methyl-1H-indol-2-yl)carbonyl]amino]-1H-inden-1-yl]-2-hydroxy-N1-methyl-, (2S)- (9CI) (CA INDEX NAME)

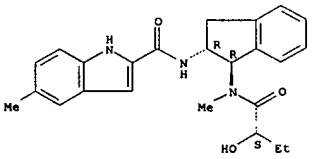
Absolute stereochemistry.



RN 846542-63-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-2,3-dihydro-1-[[(2S)-2-hydroxy-1-oxobutyl]methylamino]-1H-inden-2-yl]-5-methyl- (9CI) (CA INDEX NAME)

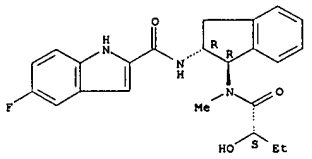
Absolute stereochemistry.

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



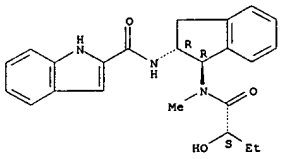
RN 846542-64-1 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-2,3-dihydro-1-[[(2S)-2-hydroxy-1-oxobutyl]methylamino]-1H-inden-2-yl]-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 846542-65-2 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-2,3-dihydro-1-[[(2S)-2-hydroxy-1-oxobutyl]methylamino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

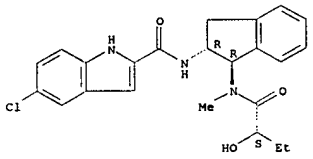
Absolute stereochemistry.



RN 846542-67-4 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[[(2S)-2-hydroxy-1-oxobutyl]methylamino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

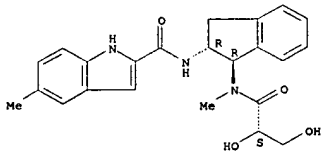
L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



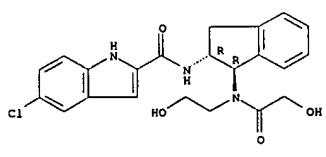
RN 846542-68-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-[[(2S)-2,3-dihydroxy-1-oxopropyl]methylamino]-2,3-dihydro-1H-inden-2-yl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 846542-69-6 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[(hydroxyacetyl)(2-hydroxyethyl)amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

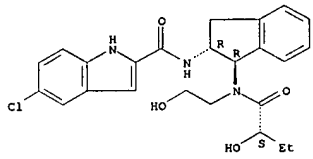
Absolute stereochemistry.



RN 846542-70-9 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[(2-hydroxyethyl)[(2S)-2-hydroxy-1-oxobutyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

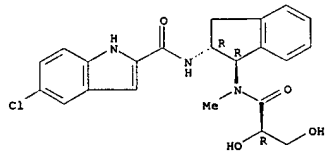
L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.



RN 846542-71-0 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-1-[[(2R)-2,3-dihydroxy-1-oxopropyl]methylamino]-2,3-dihydro-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

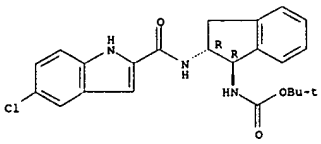


IT 597555-50-5P 846542-72-1P 846542-73-2P
846542-74-3P 846542-75-4P 846542-76-5P
846542-77-6P 846542-78-7P 846542-79-8P
846542-80-1P 846542-81-2P 846542-82-3P
846542-83-4P 846542-84-5P 846542-85-6P
846542-86-7P 846542-87-8P 846542-88-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of indole-2-carboxamide derivs. as glycogen phosphorylase inhibitors)

RN 597555-50-5 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

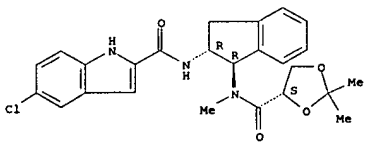
Absolute stereochemistry.

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



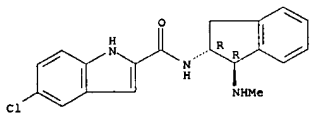
RN 846542-72-1 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-1-[[[(4S)-2,2-dimethyl-1,3-dioxolan-4-yl]carbonyl]methylamino]-2,3-dihydro-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 846542-73-2 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-(methylamino)-1H-inden-2-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

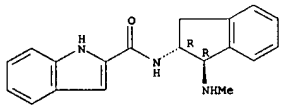
Absolute stereochemistry.



● HCl

RN 846542-74-3 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-

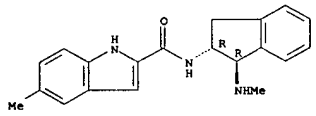
L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



● HCl

RN 846542-77-6 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-2,3-dihydro-1-(methylamino)-1H-inden-2-yl]-5-methyl-, monohydrochloride (9CI) (CA INDEX NAME)

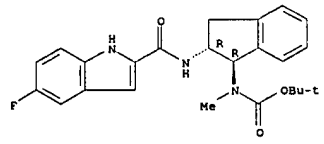
Absolute stereochemistry.



● HCl

RN 846542-78-7 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[(5-fluoro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

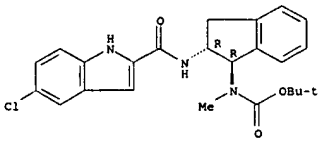
Absolute stereochemistry.



RN 846542-79-8 CAPLUS
CN Carbamic acid, [(1R,2R)-2,3-dihydro-2-[(1H-indol-2-ylcarbonyl)amino]-1H-inden-1-yl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

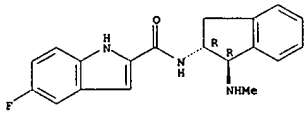
L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
dihydro-1H-inden-1-yl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 846542-75-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-2,3-dihydro-1-(methylamino)-1H-inden-2-yl]-5-fluoro-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

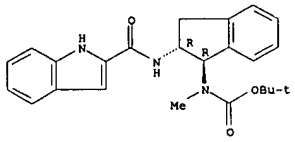


● HCl

RN 846542-76-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-2,3-dihydro-1-(methylamino)-1H-inden-2-yl]-, monohydrochloride (9CI) (CA INDEX NAME)

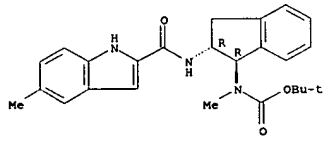
Absolute stereochemistry.

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Absolute stereochemistry.



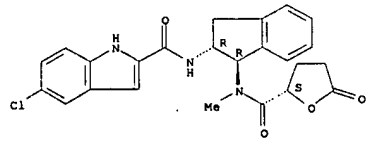
RN 846542-80-1 CAPLUS
CN Carbamic acid, [(1R,2R)-2,3-dihydro-2-[[(5-methyl-1H-indol-2-yl)carbonyl]amino]-1H-inden-1-yl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 846542-81-2 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[methyl[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

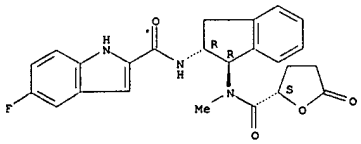
Absolute stereochemistry.



RN 846542-82-3 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-2,3-dihydro-1-[methyl[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]amino]-1H-inden-2-yl]-5-fluoro- (9CI) (CA INDEX NAME)

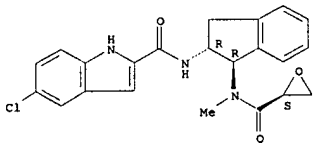
Absolute stereochemistry.

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



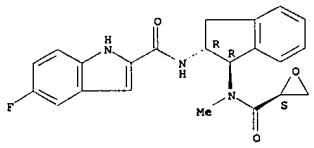
RN 846542-83-4 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[methyl[(2S)-oxiranylcarbonyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



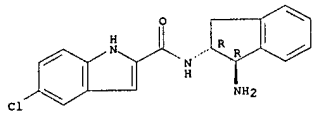
RN 846542-84-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-2,3-dihydro-1-[methyl[(2S)-oxiranylcarbonyl]amino]-1H-inden-2-yl]-5-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 846542-85-6 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[[(2S)-2-hydroxy-1-oxobutyl][2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

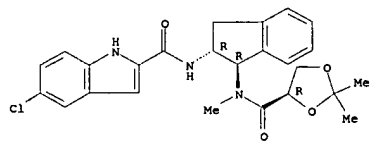


CM 2

CRN 76-05-1
CMF C2 H F3 O2

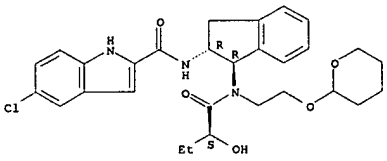
RN 846542-88-9 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-1-[[[(4R)-2,2-dimethyl-1,3-dioxolan-4-yl]carbonyl]methylamino]-2,3-dihydro-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



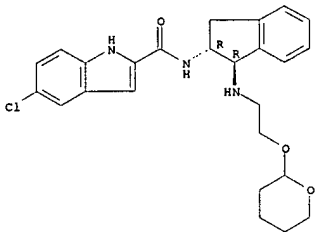
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
Absolute stereochemistry.



RN 846542-86-7 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[[2-[(tetrahydro-2H-pyran-2-yl)oxy]ethyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 846542-87-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-amino-2,3-dihydro-1H-inden-2-yl]-5-chloro-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

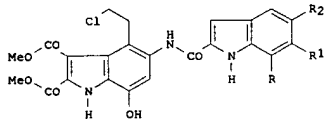
CM 1

CRN 597554-85-3
CMF C18 H16 Cl N3 O

Absolute stereochemistry.

L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:1068273 CAPLUS
DOCUMENT NUMBER: 142:240216
TITLE: Design, synthesis, and biological evaluation of achiral analogs of duocarmycin SA
AUTHOR(S): Daniell, Kristen; Stewart, Michelle; Madsen, Erik; Le, Minh; Handl, Heather; Brooks, Natalie; Kiakos, Konstantinos; Hartley, John A.; Lee, Moses
CORPORATE SOURCE: Department of Chemistry, Furman University, Greenville, SC, 29613, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2005), 15(1), 177-180
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 142:240216
GI



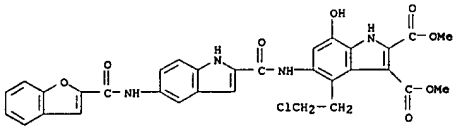
I

AB The design, synthesis, as well as biochem. and biol. evaluation of two novel achiral analogs I (R = R1 = H, R2 = NHCOR3, R3 = benzofuran-2-yl; R = R1 = R2 = OMe) of duocarmycin SA (DUMSA) were described. Like CC-1065 and adozelesin, compds. I covalently reacted with adenine-N3 in AT-rich sequences and led to the formation of DNA strand breaks upon heating. The cytotoxicity of compds. I against human cancer cells (K562, LS174T) was determined using a MTT assay giving IC50 values in the low nanomolar. Further cytotoxicity screening of I (R = R1 = R2 = OMe) conducted by the NCI against a panel of 60 different human cancer cell lines indicated that it was particularly active against several solid tumor cells lines derived from the lung, colon, CNS, skin, and breast.

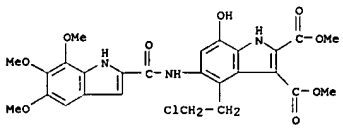
IT **413577-11-4P 413577-13-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and cancer cell cytotoxicity of duocarmycin SA analogs)

RN 413577-11-4 CAPLUS
CN 1H-Indole-2,3-dicarboxylic acid, 5-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]amino]-4-(2-chloroethyl)-7-hydroxy-, dimethyl ester (9CI) (CA INDEX NAME)

L7 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 413577-13-6 CAPLUS
CN 1H-Indole-2,3-dicarboxylic acid, 4-(2-chloroethyl)-7-hydroxy-5-[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)



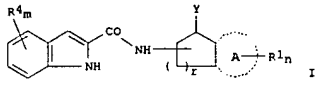
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:719447 CAPLUS
DOCUMENT NUMBER: 139:245895
TITLE: Preparation of indolamide derivatives that possess glycogen phosphorylase inhibitory activity
INVENTOR(S): Whittamore, Paul Robert Owen; Bennett, Stuart Norman Lile; Simpson, Iain
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074484	A1	20030912	WO 2003-GB883	20030304
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2477717	AA	20030912	CA 2003-2477717	20030304
AU 2003216988	A1	20030916	AU 2003-216988	20030304
BR 2003008144	A	20041207	BR 2003-8144	20030304
EP 1483240	A1	20041208	EP 2003-712310	20030304
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005107362	A1	20050519	US 2003-506554	20030304
JP 2005524667	T2	20050818	JP 2003-572954	20030304
NO 2004004032	A	20041005	NO 2004-4032	20040924
PRIORITY APPLN. INFO.:			GB 2002-5176 A	20020306
			WO 2003-GB883 W	20030304

OTHER SOURCE(S): MARPAT 139:245895
GI



Instant Application

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

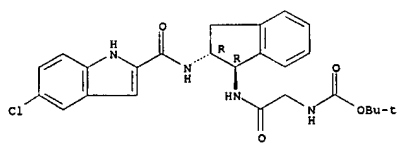
AB Heterocyclic amides of formula (I; 5-chloro-2-[N-(1-hydroxyindan-2-yl)carbamoyl]indole; A is phenylene or heteroarylene; m is 0, 1 or 2; n is 0, 1 or 2; R1 = for example halo, nitro, cyano, hydroxy, carboxy; r is 1 or 2; Y is -NR2R3 or -OR3; R2 and R3 = for example H, hydroxy, aryl, heterocyclyl and C1-4 alkyl((un)substituted by 1 or 2 R8 groups); R4 = for example H, halo, nitro, cyano, hydroxy, C1-4 alkyl, and C1-4 alkanoyl; R8 = for example hydroxy, -COCOOR9, -C(O)N(R9)(R10), -NHC(O)R9 , (R9)(R10)N- and -COOR9; R9 and R10 = for example H, hydroxy, C1-4 alkyl((un)substituted by 1 or 2 R13); R13 = hydroxy, halo, trihalomethyl and C1-4 alkoxy) or a pharmaceutically acceptable salt or prodrug thereof are claimed. They possess glycogen phosphorylase inhibitory activity and accordingly have value in the treatment of disease states associated with increased glycogen phosphorylase activity, e.g. type 2 diabetes, insulin resistance, syndrome X, hyperinsulinemia, hyperglucagonemia, cardiac ischemia, obesity. Inhibitory activity (IC50) of I in the direction of glycogen synthesis and on glycogen degradation were measure and are generally 100 μM to 1 nM; 7.4 μM for 5-chloro-N-{(1R,2R)-1-[[[(2-hydroxyethyl)(phenylmethyl)amino]acetyl]amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide in the latter assay. Processes for the manufacture of said heterocyclic amide derivs. and pharmaceutical compns. containing them are described. Thirty-seven example prepns. and/or characterization data for I and 11 for intermediates are included. For example, to prepare 5-chloro-2-[N-(trans-1-hydroxyindan-2-yl)carbamoyl]indole, 5-chloro-1H-indole-2-carboxylic acid (0.67 mmol) was dissolved in CH2Cl2 (10 mL) containing DIPEA (1.19 mmol) and trans-2-aminoindan-1-ol (0.67 mmol) and HATU (0.67 mmol); the reaction mixture was stirred at room temperature for .apprx.18 h; workup gave 100 % of the desired compound To prepare trans-2-aminoindan-1-ol, isoamyl nitrite (108 mmol) was added to a solution of indan-1,2-dione (90 mmol) in MeOH (380 mL) at 45° followed by concentrated HCl (12 mL) dropwise over 5 min; the reaction mixture was stirred for 3 h at room temperature; workup gave indan-1,2-dione-2-oxime (43%), which (39 mmol) in EtOH (470 mL) and 4M HCl/dioxane (36 mL) was hydrogenated at room temperature and 40 psi; workup gave 86 % of the trans-2-aminoindan-1-ol.

IT **597554-89-7P**, 5-Chloro-N-[(1R,2R)-1-(tert-butoxycarbonylaminoacetamido)-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide **597554-91-1P**, N-{(1R,2R)-1-[[(S)-3-[(tert-Butoxycarbonyl)amino]-4-oxopentanoyl]amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro-1H-indole-2-carboxamide **597555-23-2P**, 5-Chloro-N-[1-[(cyanomethyl)amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide **597555-25-4P**, N-[(1R,2R)-1-[(2-Amino-2-oxoethyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro-1H-indole-2-carboxamide **597555-37-8P**, N-[(1R,2R)-1-[N-(2-Acetoxyacetyl)-N-(carboxymethyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-carboxamide
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; prepn. of indolamide derivs. that possess glycogen phosphorylase inhibitory activity)

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

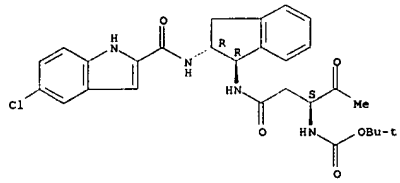
RN 597554-89-7 CAPLUS
CN Carbamic acid, [2-[[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]amino]-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

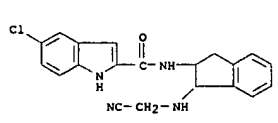


RN 597554-91-1 CAPLUS
CN Carbamic acid, [(1S)-1-acetyl-3-[[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]amino]-3-oxopropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

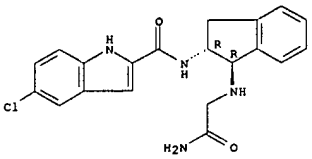


RN 597555-23-2 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[1-[(cyanomethyl)amino]-2,3-dihydro-1H-inden-2-yl]- (9CI) (CA INDEX NAME)



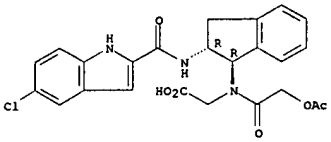
L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 597555-25-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-[(2-amino-2-oxoethyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597555-37-8 CAPLUS
CN Glycine, N-[(acetyloxy)acetyl]-N-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]- (9CI) (CA INDEX NAME)

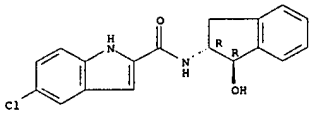
Absolute stereochemistry.



IT 597554-72-8P, 5-Chloro-2-[N-(trans-1-hydroxyindan-2-yl)carbamoyl]indole 597554-75-1P, 5-Chloro-N-[(1R,2R)-1-[(methylsulfonyl)amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597554-79-5P, N-[(1R*,2R*)-1-[(2-Carboxyacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-carboxamide 597554-83-1P, 5-Chloro-N-[(1R,2R)-1-[(3-methoxypropanoyl)amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597554-87-5P, N-[(1R,2R)-1-(Acetylamino)-2,3-dihydro-1H-inden-2-yl]-5-chloro-1H-indole-2-carboxamide 597554-93-3P, N-[(1R,2R)-1-[(2-Carbamoylacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-carboxamide 597554-95-5P, N-[(1R,2R)-1-[(2-Carboxyacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-carboxamide 597554-97-7P, 5-Chloro-N-[(1R,2R)-1-[(hydroxyacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597554-98-8P, 5-Chloro-N-[(1R,2R)-1-[[3-hydroxy-2-(hydroxymethyl)propanoyl]amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597555-00-5P, N-[(1R,2R)-1-[((3R)-3-Amino-3-carbamoylpropanoyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-

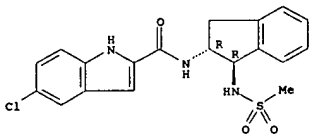
L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-hydroxy-1H-inden-2-yl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



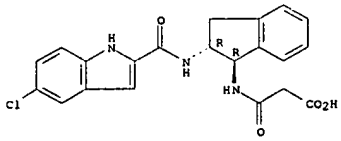
RN 597554-75-1 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[(methylsulfonyl)amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597554-79-5 CAPLUS
CN Propanoic acid, 3-[[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]amino]-3-oxo-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 597554-83-1 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[(3-methoxy-1-oxopropyl)amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
carboxamide 597555-01-6P, N-[(1R,2R)-1-[((3R)-3-Amino-3-carbamoylpropanoyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-carboxamide trifluoroacetate 597555-02-7P 597555-03-8P
,
N-[(1R,2R)-1-[(Aminoacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro-1H-indole-2-carboxamide trifluoroacetate 597555-05-0P, 5-Chloro-N-[(1S,2S)-1-[(methylsulfonyl)amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597555-08-3P, 5-Chloro-N-[1-[(hydroxyacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597555-11-8P, 5-Chloro-N-[(1R,2R)-1-[[[(2-hydroxyethyl)(methyl)amino]acetyl]amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597555-12-9P, 5-Chloro-N-[(1R,2R)-1-[[[(2-

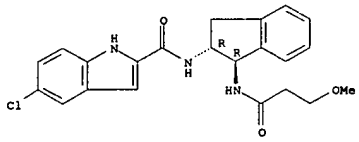
hydroxyethyl)(phenylmethyl)amino]acetyl]amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597555-13-0P, 5-Chloro-N-[(1R,2R)-1-[[(3-

hydroxypiperidin-1-yl)acetyl]amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597555-14-1P, 5-Chloro-N-[(1R,2R)-1-[[(3-

hydroxypyrrolidin-1-yl)acetyl]amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597555-15-2P, N-[(1R,2R)-1-[[(Bis(2-hydroxyethyl)amino)acetyl]amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro-1H-indole-2-carboxamide 597555-18-5P, N-[1-[(Aminoacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro-1H-indole-2-carboxamide 597555-19-6P, N-[1-[((3S)-3-Amino-3-carboxypropanoyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-carboxamide 597555-20-9P , 5-Chloro-N-[(1R,2R)-1-[[(chloromethyl)sulfonyl]amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597555-22-1P, 5-Chloro-N-[1-[[(trifluoromethyl)sulfonyl]amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597555-24-3P, 5-Chloro-N-[(1R,2R)-1-[[(1H-tetrazol-5-yl)methyl]amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597555-26-5P, N-[(1R,2R)-1-[(Carboxymethyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-carboxamide 597555-28-7P, N-[(1S,2S)-1-[Acetyl[(2-thienyl)methyl]amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro-1H-indole-2-carboxamide 597555-30-1P, N-[(1S,2S)-1-[N-Acetyl-N-(carboxymethyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-carboxamide 597555-31-2P , N-[(1S,2S)-1-[N-Acetyl-N-[[2-(ethoxycarbonyl)cycloprop-1-yl]methyl]amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-carboxamide 597555-32-3P, N-[(1R,2R)-1-[N-Acetyl-N-(carboxymethyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-carboxamide 597555-34-5P , N-[(1R,2R)-1-[Bis(carboxymethyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloroindole-2-carboxamide 597555-35-6P, N-[(1R,2R)-1-

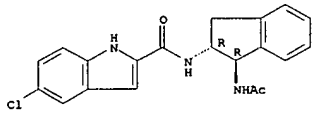
[(Acetyl)(2-amino-2-oxoethyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro-1H-indole-2-carboxamide 597555-43-6P, 5-Chloro-N-[(1R,2R)-1-[((2R)-2,3-dihydroxypropyl)amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide 597555-61-8P, 5-Chloro-2-[N-(1-hydroxyindan-2-yl)carbamoyl]indole
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of indolamide derivs. that possess glycogen phosphorylase inhibitory activity)
RN 597554-72-8 CAPLUS

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



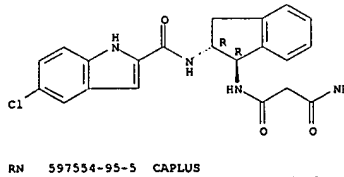
RN 597554-87-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-(acetylamino)-2,3-dihydro-1H-inden-2-yl]-5-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597554-93-3 CAPLUS
CN Propanediamide, N-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]- (9CI) (CA INDEX NAME)

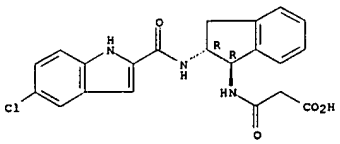
Absolute stereochemistry.



RN 597554-95-5 CAPLUS
CN Propanoic acid, 3-[[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]amino]-3-oxo- (9CI) (CA INDEX NAME)

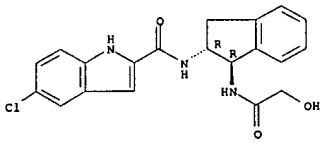
Absolute stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



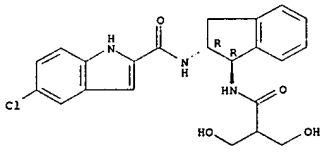
RN 597554-97-7 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[(hydroxyacetyl)amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597554-98-8 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[[3-hydroxy-2-(hydroxymethyl)-1-oxopropyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

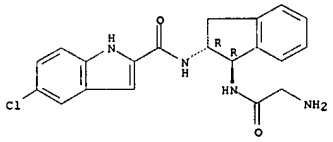


RN 597555-00-5 CAPLUS
CN Butanediamide, 2-amino-N4-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-, (2R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.

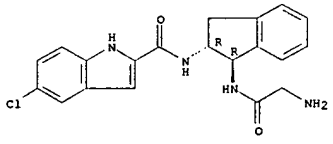


RN 597555-03-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-[(aminoacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 597555-02-7
CMF C20 H19 Cl N4 O2

Absolute stereochemistry.



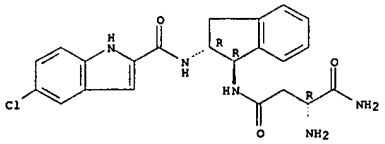
CM 2

CRN 76-05-1
CMF C2 H F3 O2

RN 597555-05-0 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1S,2S)-2,3-dihydro-1-[(methylsulfonyl)amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

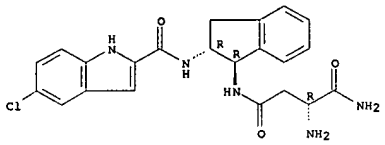


RN 597555-01-6 CAPLUS
CN Butanediamide, 2-amino-N4-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-, (2R)-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 597555-00-5
CMF C22 H22 Cl N5 O3

Absolute stereochemistry.

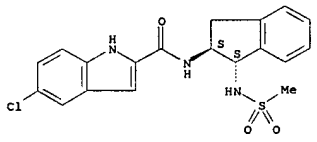


CM 2

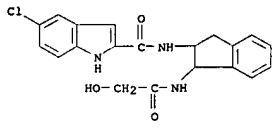
CRN 76-05-1
CMF C2 H F3 O2

RN 597555-02-7 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-[(aminoacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro- (9CI) (CA INDEX NAME)

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

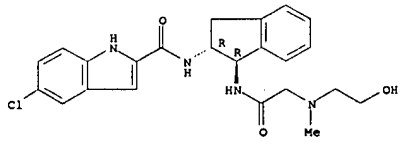


RN 597555-08-3 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2,3-dihydro-1-[(hydroxyacetyl)amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)



RN 597555-11-8 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[[[(2-hydroxyethyl)methylamino]acetyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

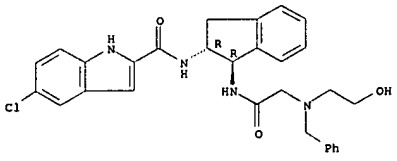


RN 597555-12-9 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[[[(2-hydroxyethyl)(phenylmethyl)amino]acetyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

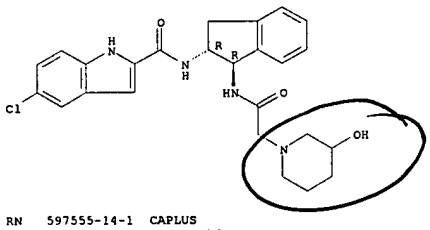
C07D 209/30
548/492
514/419
A61K 31/404



RN 597555-13-0 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[[(3-hydroxy-1-piperidinyl)acetyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

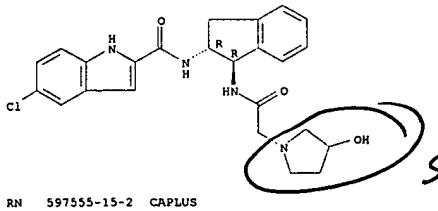
C07D 401/12
546/201
A61K 31/454
514/323



RN 597555-14-1 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[[(3-hydroxy-1-pyrrolidinyl)acetyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

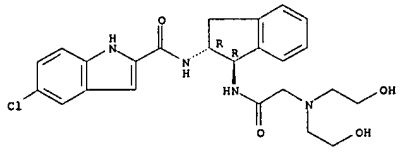
L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



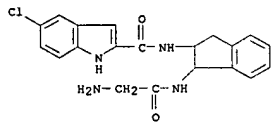
Same

RN 597555-15-2 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-[[[bis(2-hydroxyethyl)amino]acetyl]amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



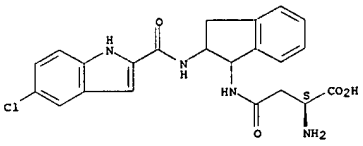
RN 597555-18-5 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[(aminoacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro- (9CI) (CA INDEX NAME)



RN 597555-19-6 CAPLUS
CN L-Asparagine, N-[2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]- (9CI) (CA INDEX NAME)

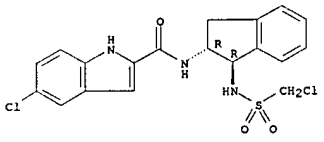
L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.

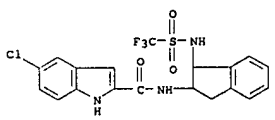


RN 597555-20-9 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-1-[[(chloromethyl)sulfonyl]amino]-2,3-dihydro-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597555-22-1 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[2,3-dihydro-1-[[(trifluoromethyl)sulfonyl]amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

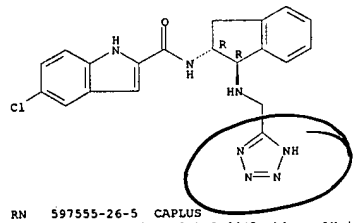


RN 597555-24-3 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-2,3-dihydro-1-[(1H-tetrazol-5-ylmethyl)amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

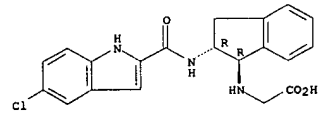
L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

514/381
A61K 31/41
C07D 257/04
548/254



RN 597555-26-5 CAPLUS
CN Glycine, N-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]- (9CI) (CA INDEX NAME)

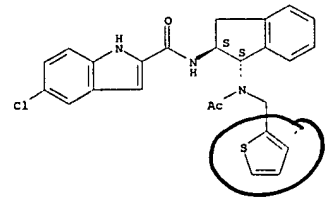
Absolute stereochemistry.



RN 597555-28-7 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2S)-1-[acetyl(2-thienylmethyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

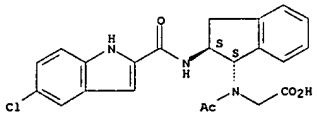
548/467
514/414



RN 597555-30-1 CAPLUS
CN Glycine, N-acetyl-N-[(1S,2S)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]- (9CI) (CA INDEX NAME)

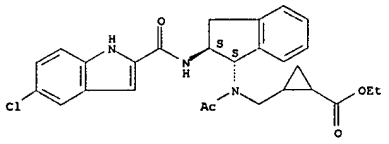
Absolute stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



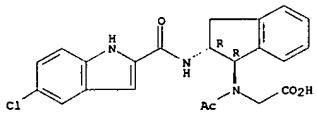
RN 597555-31-2 CAPLUS
CN Cyclopropanecarboxylic acid, 2-[[acetyl[(1S,2S)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]amino]methyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597555-32-3 CAPLUS
CN Glycine, N-acetyl-N-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]- (9CI) (CA INDEX NAME)

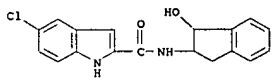
Absolute stereochemistry.



RN 597555-34-5 CAPLUS
CN Glycine, N-(carboxymethyl)-N-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



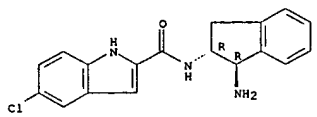
IT **597554-81-9P**, N-(trans-1-Amino-2,3-dihydro-1H-inden-2-yl)-5-chloro-1H-indole-2-carboxamide **597554-85-3P**, N-((1R,2R)-1-Amino-2,3-dihydro-1H-inden-2-yl)-5-chloro-1H-indole-2-carboxamide **597555-09-4P**, 5-Chloro-N-[1-[(iodoacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide **597555-10-7P**,

5-Chloro-N-[(1R,2R)-1-[(chloroacetyl)amino]-2,3-dihydro-1H-inden-2-yl]-1H-indole-2-carboxamide **597555-17-4P**, N-(1-Amino-2,3-dihydro-1H-inden-2-yl)-5-chloro-1H-indole-2-carboxamide trifluoroacetate **597555-21-0P**, N-((1R,2R)-1-Amino-2,3-dihydro-1H-inden-2-yl)-5-chloro-1H-indole-2-carboxamide trifluoroacetate **597555-27-6P**, 1,1-Dimethylethyl
2-[((1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]amino]acetate **597555-29-8P**, N-((1S,2S)-1-Amino-2,3-dihydro-1H-inden-2-yl)-5-chloro-1H-indole-2-carboxamide **597555-33-4P**, 1,1-Dimethylethyl 2-[acetyl[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]amino]acetate **597555-39-0P**, 1,1-Dimethylethyl

2-[[(acetyloxy)acetyl][(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]amino]acetate **597555-46-9P**, 5-Chloro-2-[N-[1-[(N-(1,1-dimethylethoxy)carbonyl]amino]indan-2-yl]carbamoyl]indole **597555-50-5P**, tert-Butyl

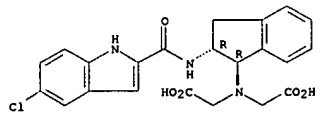
[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]carbamate **597555-53-8P**, tert-Butyl [(1S,2S)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]carbamate **597555-59-4P 597556-42-8P**, N-((1S,2S)-1-Amino-2,3-dihydro-1H-inden-2-yl)-5-chloro-1H-indole-2-carboxamide trifluoroacetate
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of indolamide derivs. that possess glycogen phosphorylase inhibitory activity)
RN 597554-81-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-amino-2,3-dihydro-1H-inden-2-yl]-5-chloro-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



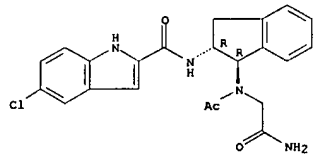
RN 597554-85-3 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-amino-2,3-dihydro-1H-inden-2-yl]-5-chloro- (9CI) (CA INDEX NAME)

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



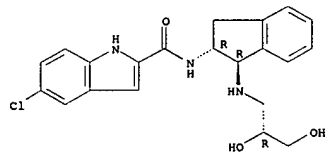
RN 597555-35-6 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-[acetyl(2-amino-2-oxoethyl)amino]-2,3-dihydro-1H-inden-2-yl]-5-chloro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597555-43-6 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-1-[[(2R)-2,3-dihydroxypropyl]amino]-2,3-dihydro-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

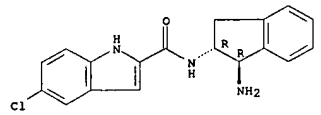
Absolute stereochemistry.



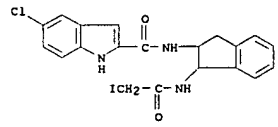
RN 597555-61-8 CAPLUS
CN 1H-Indole-2-carboxamide,
5-chloro-N-(2,3-dihydro-1-hydroxy-1H-inden-2-yl)- (9CI) (CA INDEX NAME)

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

Absolute stereochemistry.

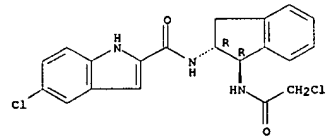


RN 597555-09-4 CAPLUS
CN 1H-Indole-2-carboxamide,
5-chloro-N-[2,3-dihydro-1-[(iodoacetyl)amino]-1H-inden-2-yl]- (9CI) (CA INDEX NAME)



RN 597555-10-7 CAPLUS
CN 1H-Indole-2-carboxamide, 5-chloro-N-[(1R,2R)-1-[(chloroacetyl)amino]-2,3-dihydro-1H-inden-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

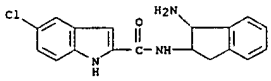


RN 597555-17-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-(1-amino-2,3-dihydro-1H-inden-2-yl)-5-chloro-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 597555-16-3
CMF C18 H16 Cl N3 O

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



CM 2

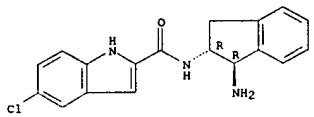
CRN 76-05-1
CMF C2 H F3 O2

RN 597555-21-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1R,2R)-1-amino-2,3-dihydro-1H-inden-2-yl]-5-chloro-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 597554-85-3
CMF C18 H16 Cl N3 O

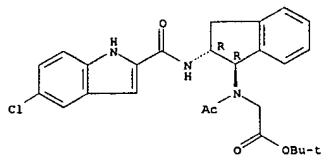
Absolute stereochemistry.



CM 2

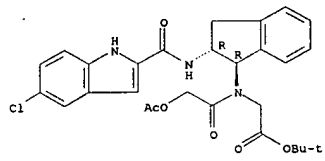
CRN 76-05-1
CMF C2 H F3 O2

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

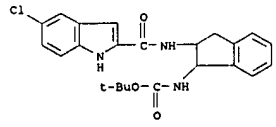


RN 597555-39-0 CAPLUS
CN Glycine, N-[(acetyloxy)acetyl]-N-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597555-46-9 CAPLUS
CN Carbamic acid, [2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



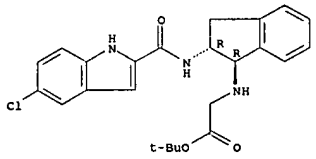
RN 597555-50-5 CAPLUS
CN Carbamic acid, [(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

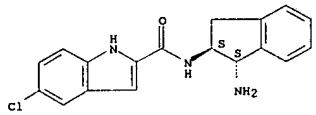
RN 597555-27-6 CAPLUS
CN Glycine, N-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597555-29-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2S)-1-amino-2,3-dihydro-1H-inden-2-yl]-5-chloro- (9CI) (CA INDEX NAME)

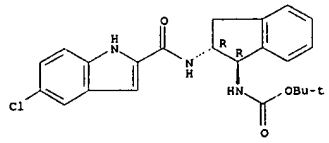
Absolute stereochemistry.



RN 597555-33-4 CAPLUS
CN Glycine, N-acetyl-N-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

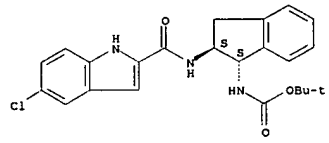
Absolute stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



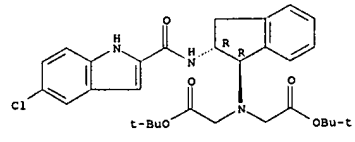
RN 597555-53-8 CAPLUS
CN Carbamic acid, [(1S,2S)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 597555-59-4 CAPLUS
CN Glycine, N-[(1R,2R)-2-[[(5-chloro-1H-indol-2-yl)carbonyl]amino]-2,3-dihydro-1H-inden-1-yl]-N-[2-(1,1-dimethylethoxy)-2-oxoethyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



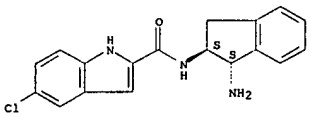
RN 597556-42-8 CAPLUS
CN 1H-Indole-2-carboxamide, N-[(1S,2S)-1-amino-2,3-dihydro-1H-inden-2-yl]-5-chloro-, trifluoroacetate (9CI) (CA INDEX NAME)

CM 1

CRN 597555-29-8
CMF C18 H16 Cl N3 O

Absolute stereochemistry.

L7 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



CM 2

CRN 76-05-1
CMF C2 H F3 O2

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:300621 CAPLUS
DOCUMENT NUMBER: 138:321053
TITLE: Methods of preparation of achiral analogs of CC-1065 and the duocarmycins and compositions thereof for use in cancer therapy
INVENTOR(S): Lee, Moses
PATENT ASSIGNEE(S): Taiho Pharmaceutical Co., Ltd., USA
SOURCE: U.S. Pat. Appl. Publ., 65 pp., Cont.-in-part of U.S. Ser. No. 666,160.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003073731	A1	20030417	US 2001-955062	20010919
US 6660742	B2	20031209		
PRIORITY APPLN. INFO.:			US 2000-666160	A2 20000919

OTHER SOURCE(S): MARPAT 138:321053
GI

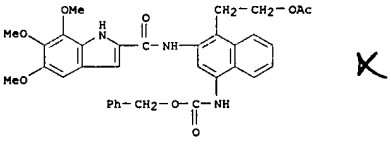
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to novel achiral seco-analogs of the DNA minor groove and sequence-selective alkylating agents (+)-CC1065 and the duocarmycins, depicted as general class I [R = CH2Ph, CO2CH2Ph, H, CO2CH2C6H4NO2-4, (4-methylpiperazin-1-yl)carbonyl; R1 = suitable minor groove binding agent, OCMe3, OCH2Ph, 9-fluorenylmethoxy, N-protecting group; R2, R3 = H, (un)branched C1-5-alkyl (e.g., Et, CH2Et, Bu, pentyl, hexyl), preferably R2 = R3 =H; R4, R5 = H, short chain alkyl, alkoxycarbonyl, preferably CO2Me, CF3; X = leaving group (Cl, Br, I, OSO2Me, OSO2C6H4Me-4, OAc, quaternary ammonium moiety, SH, C1-6-alkylsulfoxyl, C1-6-alkylsulfonyl, preferably Cl, Br, I)], II, III, IV and V. Thus, seco-analog VI was prepared from N-methyl-4-(N-methyl-4-nitropyrrole-2-carboxamido)pyrrole-2-carboxylate via hydrogenation, acylation with butyryl chloride, saponification and alkylation with 2-(2-amino-4-hydroxyphenyl)ethyl chloride. The present invention is further directed to pharmaceutical compns. thereof, and as a method for treatment of cancer using the subject compds. The cytotoxicity of VI was determined [IC50 = 12.1 μM vs. K562 leukemia cells after 1 h; IC50 = 18.0 μM vs. human colon LS174T cells after 1 h; IC50 = 82.4 μM vs. human prostate PC3 cells after 1 h; IC50 = >50.0 μM vs. human breast MCF-7 cells after 1 h; IC50 = 43 μM vs. P815 mastocytoma cells; IC50 = 23 μM vs. L1210 leukemia cells] and samples were sent to the National Cancer Institute for in-vitro screening (results included).

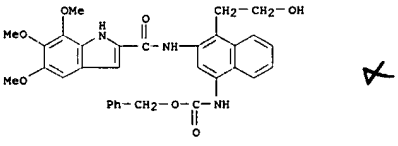
IT **413577-81-8 413577-85-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydrogenolytic debenzyloxycarbonylation of; preparation of achiral seco

L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
analogs of CC-1065 and the duocarmycins and compns. thereof for use in cancer therapy)

RN 413577-81-8 CAPLUS
CN Carbamic acid, [4-[2-(acetyloxy)ethyl]-3-[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



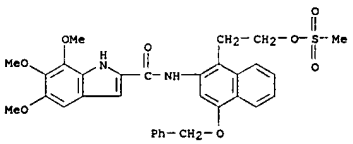
RN 413577-85-2 CAPLUS
CN Carbamic acid, [4-(2-hydroxyethyl)-3-[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



IT **413578-27-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and chlorinatino-desulfonation of; preparation of achiral seco
analogs of CC-1065 and the duocarmycins and compns. thereof for use in cancer therapy)

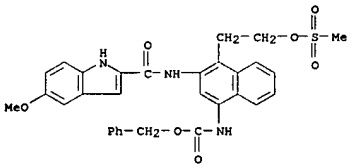
RN 413578-27-5 CAPLUS
CN 1H-Indole-2-carboxamide, 5,6,7-trimethoxy-N-[1-[2-[(methylsulfonyl)oxy]ethyl]-4-(phenylmethoxy)-2-naphthalenyl]- (9CI) (CA INDEX NAME)

L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

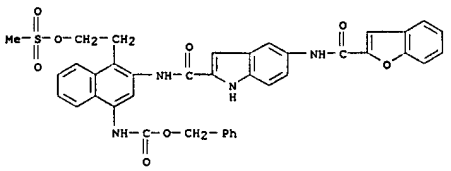


IT **413577-92-1P 413578-12-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and chlorination-desulfonation of; preparation of achiral seco
analogs of CC-1065 and the duocarmycins and compns. thereof for use in cancer therapy)

RN 413577-92-1 CAPLUS
CN Carbamic acid, [3-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-4-[2-[(methylsulfonyl)oxy]ethyl]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

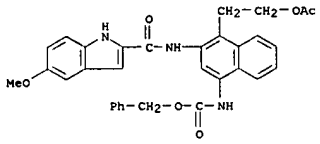


RN 413578-12-8 CAPLUS
CN Carbamic acid, [3-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]amino]-4-[2-[(methylsulfonyl)oxy]ethyl]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

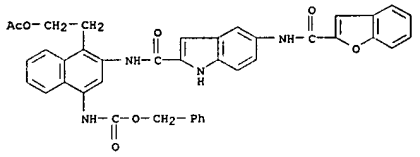


L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

IT **413577-90-9P 413578-10-6P 413578-25-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deacetylation of; preparation of achiral seco analogs of CC-1065
and the duocarmycins and compns. thereof for use in cancer therapy)
RN 413577-90-9 CAPLUS
CN Carbamic acid, [4-[2-(acetyloxy)ethyl]-3-[[[5-methoxy-1H-indol-2-yl]carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

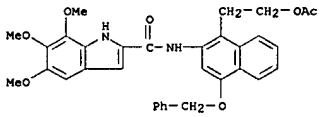


RN 413578-10-6 CAPLUS
CN Carbamic acid, [4-[2-(acetyloxy)ethyl]-3-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

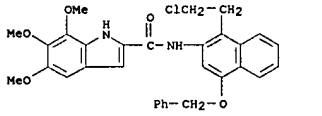


RN 413578-25-3 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[2-(acetyloxy)ethyl]-4-(phenylmethoxy)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)

L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

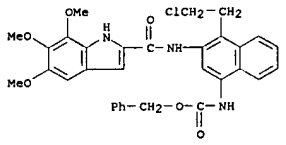


IT **413578-28-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolytic debenzylation of; preparation of achiral seco
analogs of CC-1065 and the duocarmycins and compns. thereof for use in cancer therapy)
RN 413578-28-6 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-chloroethyl)-4-(phenylmethoxy)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)

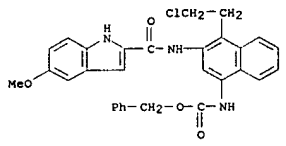


IT **413577-79-4P 413577-93-2P 413578-13-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrogenolytic debenzyloxycarbonylation of; preparation of
achiral seco analogs of CC-1065 and the duocarmycins and compns. thereof for use in cancer therapy)
RN 413577-79-4 CAPLUS
CN Carbamic acid, [4-(2-chloroethyl)-3-[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

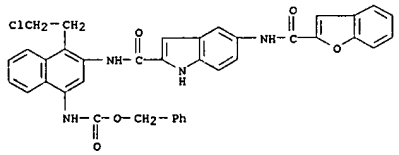
L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 413577-93-2 CAPLUS
CN Carbamic acid, [4-(2-chloroethyl)-3-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

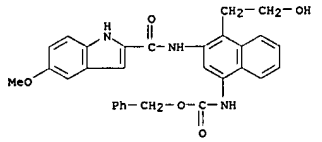


RN 413578-13-9 CAPLUS
CN Carbamic acid, [3-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]amino]-4-(2-chloroethyl)-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

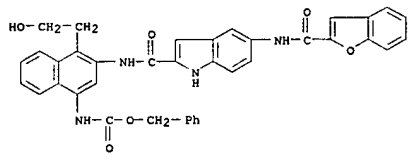


IT **413577-91-0P 413578-11-7P 413578-26-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and mesylation of; preparation of achiral seco analogs of CC-1065
and the duocarmycins and compns. thereof for use in cancer therapy)
RN 413577-91-0 CAPLUS
CN Carbamic acid, [4-(2-hydroxyethyl)-3-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX

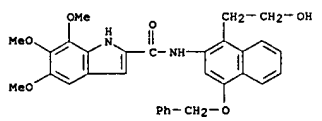
L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
NAME)



RN 413578-11-7 CAPLUS
CN Carbamic acid, [3-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]amino]-4-(2-hydroxyethyl)-1-naphthalenyl]-, phenylmethyl ester
(9CI) (CA INDEX NAME)

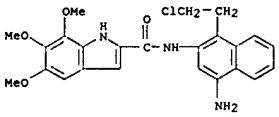


RN 413578-26-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-hydroxyethyl)-4-(phenylmethoxy)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)

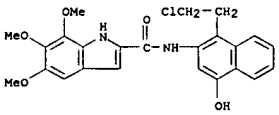


IT **413577-16-9P 413577-17-0P 413577-94-3P**
413578-14-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of achiral seco analogs of CC-1065 and the duocarmycins and
compns. thereof for use in cancer therapy)
RN 413577-16-9 CAPLUS

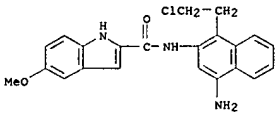
L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-chloroethyl)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



RN 413577-17-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-chloroethyl)-4-hydroxy-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)

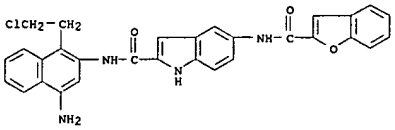


RN 413577-94-3 CAPLUS
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-chloroethyl)-2-naphthalenyl]-5-methoxy- (9CI) (CA INDEX NAME)

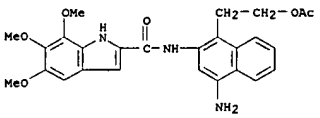


RN 413578-14-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-chloroethyl)-2-naphthalenyl]-5-[(2-benzofuranylcarbonyl)amino]- (9CI) (CA INDEX NAME)

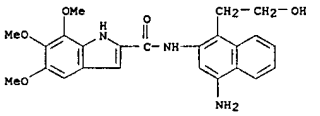
L7 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



IT **413577-83-0P 413577-87-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of achiral seco analogs of CC-1065 and the duocarmycins and
compns. thereof for use in cancer therapy)
RN 413577-83-0 CAPLUS
CN 1H-Indole-2-carboxamide,
N-[1-[2-(acetyloxy)ethyl]-4-amino-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



RN 413577-87-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-hydroxyethyl)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:293619 CAPLUS
DOCUMENT NUMBER: 136:325360
TITLE: Compositions of achiral analogs of CC-1065 and the duocarmycins and methods of the use as anticancer agents
INVENTOR(S): Lee, Moses
PATENT ASSIGNEE(S): Taiho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030894	A2	20020418	WO 2001-US29160	20010919
WO 2002030894	A3	20020620		
W: CN, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1320522	A2	20030625	EP 2001-973146	20010919
EP 1320522	B1	20051123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2004511466	T2	20040415	JP 2002-534280	20010919
AT 310724	E	20051215	AT 2001-973146	20010919
PRIORITY APPLN. INFO.:			US 2000-666160	A2 20000919
			WO 2001-US29160	W 20010919

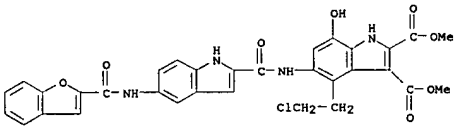
OTHER SOURCE(S): MARPAT 136:325360
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

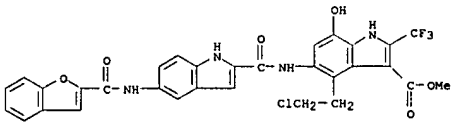
AB The present invention relates to novel achiral seco-analogs of the DNA minor groove and sequence-selective alkylating agents (+)-CC1065 and the duocarmycins, depicted as I, II, III, IV and V [X is a good leaving group, such as a Cl, Br, I, mesylate, tosylate, acetate, quaternary ammonium moiety, SH, alkylthio, alkylsulfoxyl, alkylsulfonyl; R = CH2Ph, CO2CH2Ph, H, CO2CH2C6H4NO2-4, N'-methylpiperazinyl-N-carbonyl; R1 is suitable minor groove binding agent (such as the binding units of adozelesin and duocarmycins, netropsin and bisbenzimide) to enhance the interactions of the achiral seco-cyclopropaneindole (CI) or an achiral seco-duocarmycin with specific sequences of DNA, t-butoxy, benzyloxy, 9-flurenylmethyloxy or other common protecting groups for amines; R2, R3 = H, (un)branched C1-5-alkyl, Et, Pr, Bu, pentyl, hexyl; R4, R5 = H, short alkyl, CF3, alkyloxycarbonyl, CO2Me]. Thus, I (R = H, R1 = 5,6,7-trimethoxyindole) was prepared from [4-(benzyloxy)-2-nitrophenyl]ethyl chloride via regioselective hydrogenation with H2/PtO2 in THF, N-acylation with 5,6,7-trimethoxyindole-2-carboxylic acid in CH2Cl2 containing PyBOP and EtN(CHMe2)2, followed by hydrogenolysis with H2/Pd-C in THF containing HCO2NH4. The present invention is further directed to pharmaceutical compns. thereof, and as a method for treatment of cancer using the subject

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
compds. Bioactivity of I (R = H, R1 = 5,6,7-trimethoxyindole) was detd. [IC50 = 0.37 μM vs. K562 cells; IC50 = 0.94 μM vs. PC3 cells; IC50 = 1.5 μM vs. L1210 cells; 51±3 % form I DNA alkylation and 49±4% form II DNA alkylation at 0.1 mM; gel scans in Taq polymerase stop assay are given].

IT **413577-11-4P 413577-12-5P 413577-13-6P**
413577-14-7P 413577-16-9P 413577-17-0P
413577-83-0P 413577-87-4P 413577-94-3P
413578-14-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of achiral analogs of CC-1065 and the duocarmycins as anticancer agents)
RN 413577-11-4 CAPLUS
CN 1H-Indole-2,3-dicarboxylic acid, 5-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]amino]-4-(2-chloroethyl)-7-hydroxy-, dimethyl ester (9CI) (CA INDEX NAME)

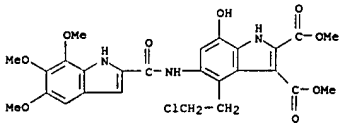


RN 413577-12-5 CAPLUS
CN 1H-Indole-3-carboxylic acid, 5-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]amino]-4-(2-chloroethyl)-7-hydroxy-2-(trifluoromethyl)-, methyl ester (9CI) (CA INDEX NAME)

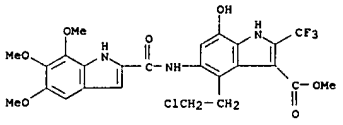


RN 413577-13-6 CAPLUS
CN 1H-Indole-2,3-dicarboxylic acid, 4-(2-chloroethyl)-7-hydroxy-5-[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-, dimethyl ester (9CI) (CA INDEX NAME)

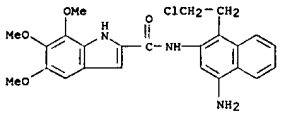
L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 413577-14-7 CAPLUS
CN 1H-Indole-3-carboxylic acid, 4-(2-chloroethyl)-7-hydroxy-2-(trifluoromethyl)-5-[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

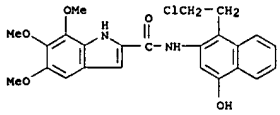


RN 413577-16-9 CAPLUS
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-chloroethyl)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)

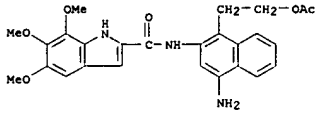


RN 413577-17-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-chloroethyl)-4-hydroxy-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)

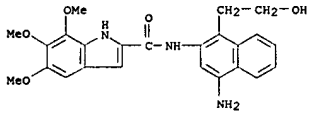
L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 413577-83-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[2-(acetyloxy)ethyl]-4-amino-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)

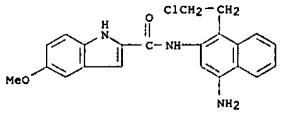


RN 413577-87-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-hydroxyethyl)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)

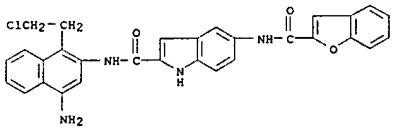


RN 413577-94-3 CAPLUS
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-chloroethyl)-2-naphthalenyl]-5-methoxy- (9CI) (CA INDEX NAME)

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

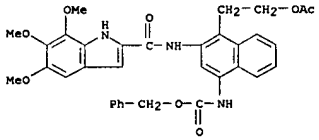


RN 413578-14-0 CAPLUS
CN 1H-Indole-2-carboxamide, N-[4-amino-1-(2-chloroethyl)-2-naphthalenyl]-5-[(2-benzofuranylcarbonyl)amino]- (9CI) (CA INDEX NAME)



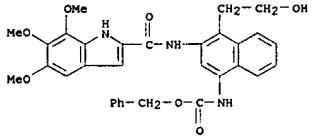
IT 413577-81-8 413577-85-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of achiral analogs of CC-1065 and the duocarmycins as anticancer agents)

RN 413577-81-8 CAPLUS
CN Carbamic acid, [4-[2-(acetyloxy)ethyl]-3-[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



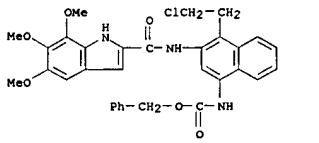
RN 413577-85-2 CAPLUS
CN Carbamic acid, [4-(2-hydroxyethyl)-3-[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

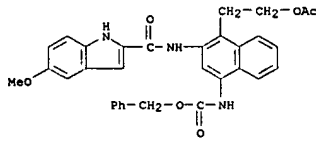


IT 413577-79-4P 413577-90-9P 413577-91-0P
413577-92-1P 413577-93-2P 413578-10-6P
413578-11-7P 413578-12-8P 413578-13-9P
413578-25-3P 413578-26-4P 413578-27-5P
413578-28-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of achiral analogs of CC-1065 and the duocarmycins as anticancer agents)

RN 413577-79-4 CAPLUS
CN Carbamic acid, [4-(2-chloroethyl)-3-[[(5,6,7-trimethoxy-1H-indol-2-yl)carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

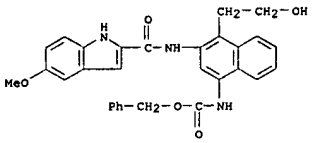


RN 413577-90-9 CAPLUS
CN Carbamic acid, [4-[2-(acetyloxy)ethyl]-3-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

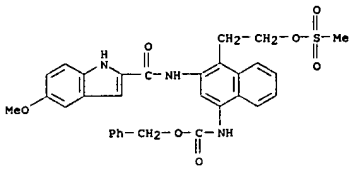


RN 413577-91-0 CAPLUS

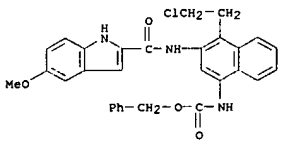
L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
CN Carbamic acid, [4-(2-hydroxyethyl)-3-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



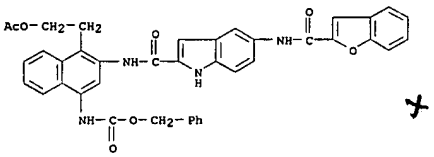
RN 413577-92-1 CAPLUS
CN Carbamic acid, [3-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-4-[2-[(methylsulfonyl)oxy]ethyl]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



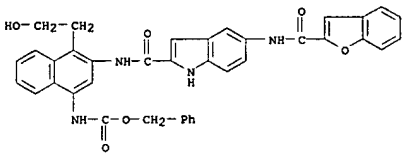
RN 413577-93-2 CAPLUS
CN Carbamic acid, [4-(2-chloroethyl)-3-[[(5-methoxy-1H-indol-2-yl)carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



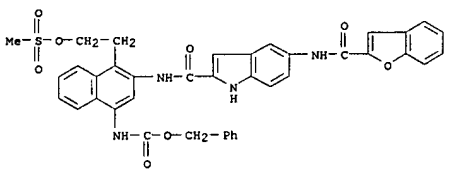
L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)
RN 413578-10-6 CAPLUS
CN Carbamic acid, [4-[2-(acetyloxy)ethyl]-3-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]amino]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



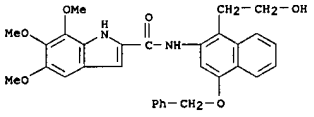
RN 413578-11-7 CAPLUS
CN Carbamic acid, [3-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]amino]-4-(2-hydroxyethyl)-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



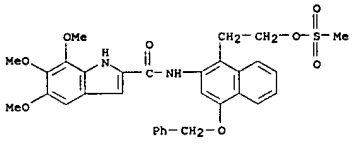
RN 413578-12-8 CAPLUS
CN Carbamic acid, [3-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]amino]-4-[2-[(methylsulfonyl)oxy]ethyl]-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



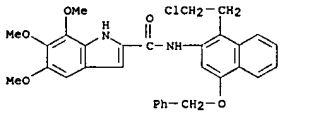
L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)



RN 413578-27-5 CAPLUS
CN 1H-Indole-2-carboxamide, 5,6,7-trimethoxy-N-[1-[2-[(methylsulfonyl)oxy]ethyl]-4-(phenylmethoxy)-2-naphthalenyl]- (9CI) (CA INDEX NAME)

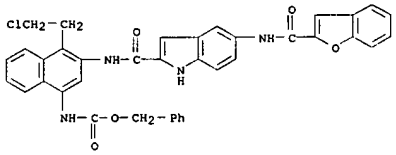


RN 413578-28-6 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-chloroethyl)-4-(phenylmethoxy)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)

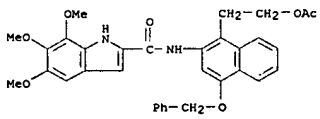


L7 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN (Continued)

RN 413578-13-9 CAPLUS
CN Carbamic acid, [3-[[[5-[(2-benzofuranylcarbonyl)amino]-1H-indol-2-yl]carbonyl]amino]-4-(2-chloroethyl)-1-naphthalenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)



RN 413578-25-3 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-[2-(acetyloxy)ethyl]-4-(phenylmethoxy)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)



RN 413578-26-4 CAPLUS
CN 1H-Indole-2-carboxamide, N-[1-(2-hydroxyethyl)-4-(phenylmethoxy)-2-naphthalenyl]-5,6,7-trimethoxy- (9CI) (CA INDEX NAME)